



Please Take a Moment to Study this Electrocardiogram: It May Help You Prevent a Sudden Death

Sami Viskin MD, Aharon Glick MD and Bernard Belhassen MD

Department of Cardiology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
 Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

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Please take a moment to review the ECG shown in Figure 1. It may help you identify patients at increased risk for arrhythmic death. This particular trace belongs to a young patient who had an out-of-hospital cardiac arrest due to ventricular fibrillation at the age of 22 years [1]. A complete cardiac evaluation failed to disclose any evidence of organic heart disease. Seven years after his successful resuscitation, he remains free of cardiac symptoms (other than recurrent arrhythmias) and has no deterioration of cardiac function. This case exemplifies the typical features of the "Brugada syndrome" [2].

Eight years ago, two Spanish cardiologists, the brothers Pedro and Josep Brugada, described the association between this peculiar electrocardiogram (showing a right bundle branch block pattern with peculiar ST-segment elevation in leads V1-V3) and the occurrence of VF in ostensibly healthy patients. In the years that followed, it became clear that this "Brugada syndrome" is responsible for a significant percentage of cases of sudden death among young adults without heart disease [3].

The Brugada syndrome is a genetic disorder. The mutations discovered so far affect the gene that encodes a human cardiac sodium channel [4-6]. The defective sodium current results in an inappropriately short action potential [7], and this action potential shortening is more marked in some areas (right ventricular epicardium) than in others [7]. The resulting "dispersion of repolarization" facilitates the onset of a malignant polymorphic ventricular tachycardia [Figure 2] that is responsible for the symptoms in the Brugada syndrome. The symptoms include syncope (when the arrhythmia terminates spontaneously) or cardiac arrest (when the polymorphic ventricular tachycardia deteriorates to VF).

The Brugada syndrome affects mainly young male adults. Although infants with symptomatic Brugada syndrome have been described [8], the majority of patients are 25-50 years old at the time of diagnosis and 85% of all symptomatic individuals are males [3]. The arrhythmias in the Brugada syndrome are not clearly related to physical or emotional stress. In fact, many patients have

arrhythmias while asleep [9,10]. These may present as nocturnal seizures or nocturnal sudden death.

The diagnosis of Brugada syndrome is straightforward when the typical ECG is observed following resuscitation from VF. In our experience, this occurs in about 25% of cardiac arrest survivors who have no evidence of organic heart disease [10], but others report figures as high as 40-60% [9,11]. On the other hand, a normal or near-normal electrocardiogram does not negate this diagnosis. This is because the ECG morphology of patients with Brugada syndrome demonstrates marked day-to-day variability and the ST segments may look normal at times. In questionable cases, a "flecainide challenge test" may help to support the diagnosis [12]. Flecainide (an anti-arrhythmic drug commonly used to treat atrial fibrillation) is a sodium-channel blocker that exposes the inborn dysfunction of sodium channels of the Brugada syndrome [12]. Brugada reported that this "flecainide challenge test" is essentially infallible for exposing the Brugada sign in patients with sodium-channel mutations [12]. More recent data, however, suggest a positive

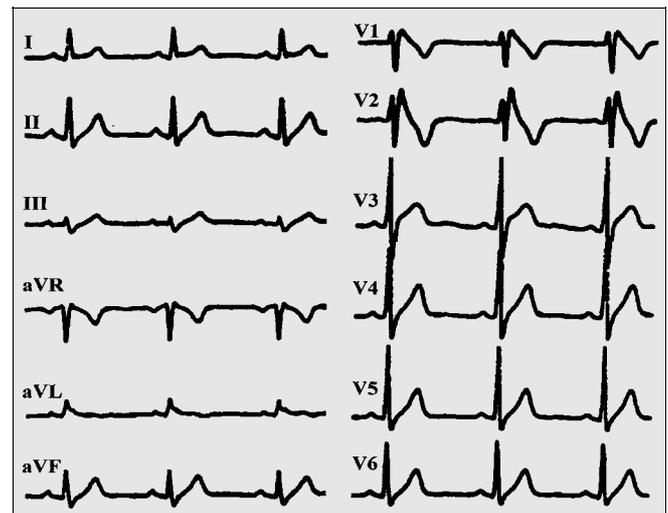


Figure 1. Electrocardiogram of a 22 year old male patient with Brugada syndrome.

VF = ventricular fibrillation

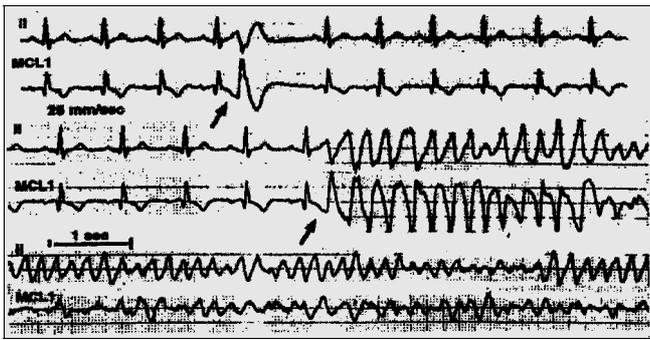


Figure 2. Recurrent bursts of spontaneous non-sustained polymorphic ventricular tachycardia in a patient with Brugada syndrome. Reproduced with permission from the *Journal of Cardiovascular Electrophysiology*.

predictive value of only 35% for patients with established sodium-channel mutations but normal ECG [13].

The implantable cardioverter defibrillator is recommended in most centers for cardiac arrest survivors with a Brugada sign. Indeed, long-term series suggest that patients with Brugada syndrome who survive a VF episode are likely to develop a second one, which can be effectively treated by the implantable cardioverter defibrillator [14]. An alternative therapy proposed by us [15] involves the use of quinidine guided by the results of electrophysiologic evaluation. By blocking potassium outflow currents, quinidine prolongs the action potential (which is inappropriately short in the Brugada syndrome) [16]. According to this approach, VF is first induced by programmed ventricular stimulation in the catheterization room. Oral quinidine is then started and a second electrophysiologic study is performed. If no ventricular arrhythmias are induced despite a very aggressive protocol of extrastimulation the patient is discharged on this therapy. The long-term experience with this approach is limited, but has been very rewarding [15].

All physicians, regardless of their field of interest, should be aware of the Brugada syndrome and should be able to recognize its electrocardiographic features. More than one patient presenting with syncope has been misdiagnosed as "vasovagal" or "epilepsy," because the peculiar ECG was not noticed, only to develop a cardiac arrest episode later on. Not all patients with a "Brugada sign" on their ECG develop symptoms, and the appropriate management of asymptomatic patients is controversial. Nevertheless, a Brugada sign should not be viewed as a "normal finding" [10] and cannot be ignored.

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Correspondence: Dr. S. Viskin, Dept. of Cardiology, Tel Aviv Sourasky Medical Center, 6 Weizmann St., Tel Aviv 64239, Israel.
Phone/Fax: (972-3) 697-4418
email: viskin_s@netvision.net.il

If you have the good fortune to command a large clinic, remember that one of your chief duties is the tabulation and analysis of the carefully recorded experience.

*William Osler (1849-1919), Canadian physician considered the "father" of modern medicine, and the first author of **Harrison's Principles of Internal Medicine***